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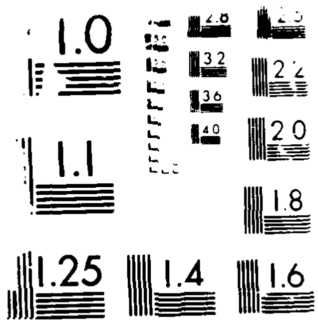
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INVESTIGATION OF BIOCHEMICAL VARIATION IN OPERATIONAL AIRCREW

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To establish whether clusters of covarying biochemical variables in "casual" morning blood samples might indicate situations or individuals marked by increased stress levels, we analyzed principal components of biochemical data on 1147 pilots and navigators, from the Clinical Sciences Division's biochemical data base (U.S. Air Force School of Aerospace Medicine). The final analysis, based on the 790 individuals with complete data, produced two factors that had apparent face validity as stress indicators. The first, Factor 1, reflected a pattern of increased RBC sedimentation rate, triglycerides, cholesterol/HDL ratio, and uric acid--a pattern that could be explained by increased levels of sympathetic nervous system activity. The second, Factor 4, reflected a pattern of increased 0900 cortisol, fasting blood sugar, and sodium/potassium ratio, with a decreased serum calcium--a pattern that could be explained by increased levels of pituitary-adrenocortical activation. Supporting the validity of these factors as stress

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19. ABSTRACT (continued)

indicators, Factor 1 scores increased significantly in both pilots and navigators as a function of increasing command status as indexed by aeronautical rating. Among pilots only, Factor 4 scores also increased significantly as a function of increasing command responsibility. These associations are diminished if controlled for age by analysis of covariance, but we believe that the relationships are not due solely to the effect of age. Initial attempts to relate levels of these two factors to plane assignment yielded promising, but inconclusive, results. We conclude that high scores on Factors 1 and 4 may reflect the increased stress levels that would be expected with increased command responsibility. Additional data and further statistical analyses will be required to confirm the validity of these initial findings. Particularly promising avenues for further investigation include 1) correlation of scores on these two factors with other measures (e.g., blood pressure responses to exercise testing; personality profiles) that reflect stress; 2) correlation of factor scores with both concurrent and subsequent morbidity and mortality, particularly forms (e.g., coronary disease) that might be potentiated by stress; and 3) evaluation of scores on the stress factors as predictors of subsequent performance in a variety of career paths (e.g., transport and bomber versus fighter and reconnaissance assignment).

SUMMARY

Principal-components analyses of biochemical values obtained on a sample of operational aircrew revealed two factors that appear to reflect stress levels: Factor 1--positive loadings for RBC sedimentation rate, serum uric acid, triglycerides, and cholesterol/HDL ratio; and Factor 4--a negative loading for serum calcium and positive loadings for 0900 plasma cortisol, fasting blood sugar, and Na/K ratio. High Factor-1 scores could result from increased sympathetic nervous system activity, and high Factor 4 scores could reflect heightened arousal of the pituitary-adrenocortical axis. Both are logical consequences of stress, whether due to chronic environmental pressures, individual characteristics predisposing to reduced stress tolerance, or some combination. The pattern of relationship between scores on these factors and individual variables such as command status and environmental variables such as aircraft type suggests that scores on Factors 1 and 4 are indeed valid indicators of stress. If further studies strengthen these conclusions, scores on these two factors may be useful measures of pilot attributes that should be routinely screened for, so as to select personnel with highest proficiency but least possible health risks.

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INVESTIGATION OF BIOCHEMICAL VARIATION IN OPERATIONAL AIRCREW

INTRODUCTION

There is considerable evidence that military personnel subjected to a wide variety of stressful assignments will exhibit higher levels of various biochemical indices in both blood and urine than when they are not under such stressful conditions or are compared to other personnel for whom the given situation should be less stressful.

For example, urinary excretion of catecholamines and 17-hydroxy-corticosteroids (17-OHCS) have been evaluated in aircrew engaged in hazardous or unusually demanding missions (1,2). The stress of initial practice of aircraft carrier landings was associated with increased blood and urinary cortisol levels in naval aviators (3). Interestingly, the corticosteroid elevations were greatest in the pilot in command of the aircraft rather than in the more passive radar-intercept officer. In a study of B-52 aircrews, 17-OHCS excretion levels were greatest in the aircraft commanders (4). Among a team of Special Forces personnel anticipating an attack upon their isolated camp by the Viet Cong, the highest 17-OHCS excretion rates were observed among the two officers rather than the enlisted personnel (5). Such findings as these led Miller et al. (3) to conclude that "the assigned role of leadership and responsibility appeared to be the major factor enhancing the physiological response...in an acutely stressful situation."

In addition to reflecting both the impact of stressful situations and the effects of such situations upon those in different roles of responsibility, biochemical indices have provided potentially useful information about performance capabilities in the stressful situation. While serum uric acid levels showed a general increase among naval personnel undergoing underwater demolition team (UDT) training, these men who failed to complete the training had lesser uric acid elevations than those who successfully completed the course; and peak uric acid levels occurred among successful trainees when they were noted to be "alert, attentive, eager for training, and trying hard to master course materials" (6). Among medical students undergoing a stressful course examination, those with the highest serum uric acid levels made the highest grades on the examination (7). One possible reason for the association between elevated uric acid and better performance and motivation is that the increased uric acid levels are caused by increased catecholamine secretion (8), which helps maintain high levels of arousal and involvement in the task at hand. On the other hand, Hale et al. (9) found lower levels of endocrine-metabolic displacement to correlate with better pilot performance.

Besides reflecting increased task involvement and better performance, however, elevations of some biochemical stress indicators may have potentially harmful effects. Troxler et al. (10) found increased plasma cortisol levels in the late morning, during the course of glucose tolerance tests, to be

associated with more severe coronary atherosclerosis among Air Force personnel undergoing coronary angiography at the USAF School of Aerospace Medicine (USAFSAM).

Most of the studies just discussed have evaluated biochemical indicators in the context of obviously stressful situations. The purpose of our investigation was to determine whether levels of potential biochemical stress indicators measured in blood samples obtained under routine clinical conditions would reflect stress effects. We used principal-components analyses with varimax rotation to identify correlated clusters of biochemical values that might qualify as possible stress indicators in blood samples obtained from a sample of operational aircrew being evaluated at the USAFSAM. Further analyses were carried out to evaluate the validity of candidate clusters, in terms of the relationship between cluster scores for each individual and his aeronautical rating and the type of aircraft flown. This report describes the statistical procedures used to identify the clusters with good potential to serve as stress indicators, along with results of the analyses evaluating the validity of these clusters as potential reflectors of stress levels.

METHODS

Subject Selection

The original data set contained 50 biochemical and hematologic variables on 1147 patients at USAFSAM. After initial editing and verification of this data set, we undertook analyses to identify patients whose data should be discarded. The four female subjects in the sample had unusual values on a number of variables. Since their physiologic responses to stress may differ from that of their male counterparts and the subgroup was too small to test for reliable differences, they were excluded from further analyses. Three male subjects with numerous extreme values suggesting exaggerated pathophysiologic states were also excluded.

All values flagged as extreme or errant were the subject of special scrutiny. Any entries associated with probable laboratory errors were deleted from the final data set.

Selection of Variables

We prepared univariate descriptive statistics for all variables to check for suspicious values and marked deviations from normality. This led to the exclusion of 12 variables due to inadequate variability, poor distributions, or large numbers of missing values. Demographic and background variables (e.g., exam date, race, flying hours) were excluded from these analyses. In addition, four variables with bimodal distributions (renal RBC, renal WBC, granulocytes, and hyaline casts) were dichotomized.

Serum sodium and potassium measures were transformed into the ratio of sodium to potassium since this is considered a better index of the stress response than either determination alone (11). Similarly, high density lipoprotein (HDL) and total cholesterol were transformed into a lipids ratio (total cholesterol/HDL).

A series of preliminary principal-components analyses with varimax rotations aided further selection of variables. These early analyses yielded a number of factors easily interpreted as specific disease syndromes (such as urinary tract infections, hepatitis, acute infection), as well as some factors more likely to be related to the stress response. Variables were excluded from subsequent analyses if they appeared to be strongly related to particular disease states and/or there was no physiologic reason to expect them to be related to a stress response.

The process of variable elimination produced a set of 11 variables with complete data for 1033 subjects. These variables were the basis of the principal-components analysis outlined in Table 1. Examination of the factor pattern revealed that two of the six factors with eigenvalues greater than 1 appeared to be related to stress. These six factors accounted for 70% of the total variance. The strongest factor in the data (Factor 1: 17% of the variance) had high loadings for RBC sedimentation rate, triglycerides, uric acid, and lipids ratio--all variables thought to reflect the sympathetic nervous system role in the stress response. Factor 4 also had loadings from stress-related variables--primarily calcium, with secondary loadings from uric acid and the sodium-potassium ratio--and appeared to reflect a physiologic pattern associated with known actions of cortisol.

TABLE 1. PRINCIPAL COMPONENTS: ROTATED FACTOR PATTERN

	Factors					
Variables	1	2	3	4	5	6
Hematocrit	.18	.82	-.05	.21	.03	-.02
Eosinophils	.00	-.01	-.01	.03	.02	.95
Sedimentation rate	.32	-.75	-.13	.20	.01	-.02
Triglycerides	.83	.01	.05	-.02	-.01	.03
Calcium	.03	-.02	-.02	.83	-.21	.04
Phosphorus	.04	.03	.78	-.01	-.12	-.21
Uric acid	.55	-.08	-.13	.24	.27	-.20
Fasting blood sugar	.17	-.03	-.73	-.01	-.10	-.21
Lipids ratio	.83	-.01	-.01	-.11	-.06	.04
Na/K ratio	.10	-.04	-.04	-.21	.82	.04
Bilirubin	-.16	.21	.07	.55	.54	-.03

We therefore decided that the unambiguous interpretation of Factor 4 required adding a measure of cortisol level to the analysis. Since cortisol measures were available on only 110 subjects in the original data set, further data were extracted from the USAFSAM files. Two cortisol indices (0700 and 0900) were obtained for a total of 722 additional subjects. We chose to include the 0900 measure in our analysis because of its past association with coronary angiographic findings (10).

The final data set consisted of 12 physiologic variables, with complete data for 790 of the original subjects.

Final Principal-Components Solution

The final principal-components analysis yielded five factors with eigenvalues greater than 1, accounting for 58% of the variance. These factors were rotated using the varimax procedure, producing the factor pattern shown in Table 2. Two appear to be good candidates as stress indicators. Factor 1--with high loadings for sedimentation rate, triglycerides, uric acid, and the lipids ratio--was the strongest factor in the data, accounting for 17% of the variance. Factor 4 accounted for 11% of the variance and included strong loadings for cortisol, calcium (-), fasting blood sugar, and the sodium/potassium ratio.

TABLE 2. PRINCIPAL COMPONENTS INCLUDING CORTISOL: ROTATED FACTOR PATTERN

	Factors				
Variables	1	2	3	4	5
Cortisol (0900)	.00	.24	.38	.48	-.10
Hematocrit	.22	.81	.20	.08	.04
Eosinophils	-.04	.10	.06	-.20	.71
Sedimentation rate	.39	-.72	.12	.06	.03
Triglycerides	.82	.01	-.07	.04	-.02
Calcium	.10	-.04	.72	-.37	.05
Phosphorus	-.02	.09	.03	-.24	-.71
Uric acid	.56	-.16	.30	.20	.00
Fasting blood sugar	.27	-.22	-.13	.41	.26
Lipids ratio	.83	.04	-.16	.05	.01
Na/K ratio	.04	.00	-.02	.73	.01
Bilirubin	-.17	.11	.67	.23	.00

Correlates of Factor Scores

To explore the potential validity of Factors 1 and 4 as indicators of the stress response, we computed individual scores on the factors and related them to duty assignment variables that might be associated with varying degrees of stress. We chose aeronautical rating as one potential indicator of job stress since it should be related to command responsibility. The mean factor scores, broken down by aeronautical rating, are presented in Table 3.

TABLE 3. FACTOR SCORES (DESCRIPTIVE STATISTICS) BY AERONAUTICAL RATING

Group	N	Mean	Variance	SE	Skewness
FACTOR 1					
Pilots					
Command	240	.28	1.18	.07	1.26
Senior	166	-.22	1.03	.08	.88
Pilot	121	-.19	.61	.07	.19
Student	37	-.22	.57	.12	.56
Navigators					
Master	95	.34	.86	.09	.65
Senior	62	-.19	.94	.12	.24
Navigator	67	-.25	.80	.11	.06
Student	2	-1.00	1.27	.80	
FACTOR 4					
Pilots					
Command	240	.13	1.04	.07	1.39
Senior	166	.06	1.00	.08	.22
Pilot	121	-.33	.80	.08	-.09
Student	37	-.27	.63	.13	-.30
Navigators					
Master	95	.08	1.14	.11	.53
Senior	62	.08	1.16	.14	.87
Navigator	67	-.05	.79	.11	-.02
Student	2	.51	3.39	1.30	

Analysis of variance reveals that factor scores of pilots do not differ from those of navigators, and there is a strong relationship between Factor 1 and aeronautical rating across pilot and navigator groups, $F(3, 785) = 17.59$, $p < .001$ (see Figure 1). This relationship apparently is a threshold effect rather than a monotonic function, with command pilots and master navigators having higher scores than the less senior aircrew. Pairwise comparisons with the Tukey test show that the command/master level differs from the other three categories ($p < .01$), which do not differ from each other. In addition, the within-cell distributions tend to show increasing amounts of positive skew in the more senior levels. This indicates that the upper levels contain more individuals with unusually high scores on Factor 1.

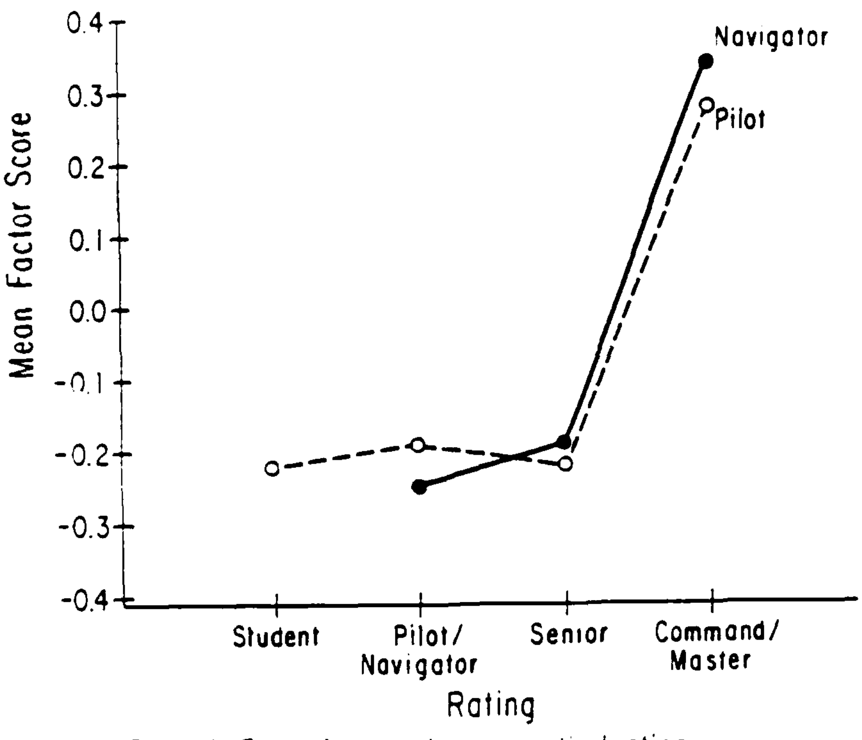

Figure 1. Factor 1 scores by aeronautical rating.

As with Factor [illegible], a two-way analysis of variance reveals that pilots do not differ from navigators on Factor 4, and scores are strongly associated with aeronautical rating, $F_{(3, [illegible])} = 5.5[illegible]$, $p < .001$. Although there is no significant interaction between status as pilot or navigator and aeronautical rating, the main effect for rating is due to the differences among the pilots (Figure 2). If the data from navigators are analyzed separately, the effect is not significant. Once again we find an apparent threshold relationship, but the division between high and low scores occurs at the boundary between pilots and senior pilots. Tukey pairwise comparisons reveal that junior pilots and navigators have lower scores than their more senior counterparts, who do not differ from each other. The comparisons of students to other categories are not significant, but this is due to the small number of cases and the presence of one student navigator with an unusually high score (1.82). As with Factor [illegible], the amount of positive skew increases with aeronautical rating.

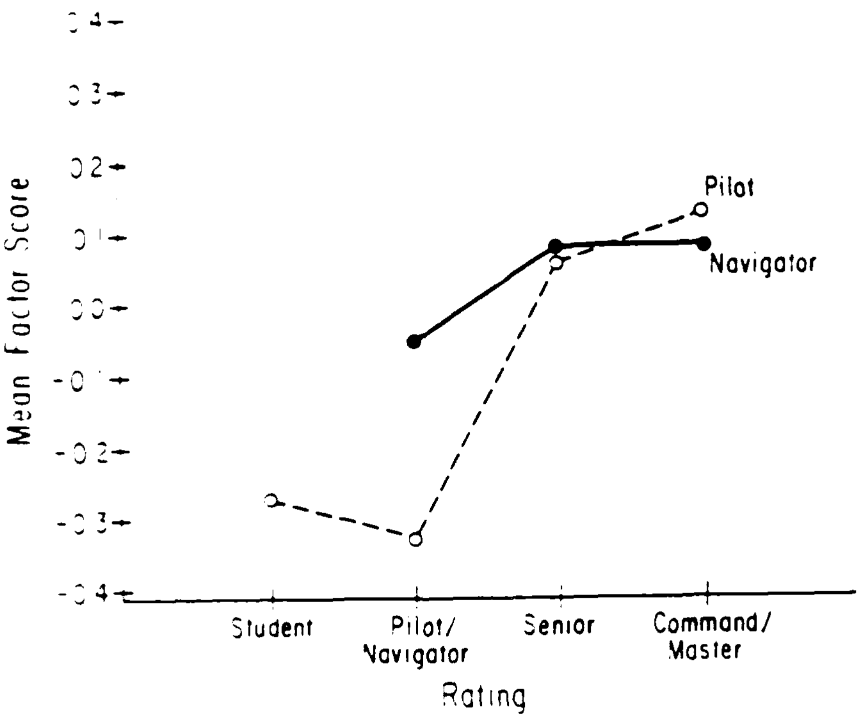

Figure 2. Factor 4 scores by aeronautical rating.

The relationship between these factor scores and status are potentially confounded with age since crewmembers more senior in command are naturally older. In fact, this relationship is so strong that we could not control for age with stratification procedures because of multiple empty cells. Adjustment for age with analysis of covariance eliminates the effect for Factor 4, but the Factor 1 effect remains significant--$F(3,784)=3.77$, $p = .01$; however, the pattern of simple effects in this analysis of adjusted Factor 1 score is difficult to interpret. Command/master-level subjects have higher scores than senior-level pilots and navigators ($p < .01$), but the scores of junior pilots and navigators no longer differ from those in any other category. Despite the fact that covariance adjustment for age attenuates the association between rating and the factor scores, we have reason to believe that the effect is not due entirely to age. For one thing, the correlations between age and factor scores within rating categories are generally low. The mean correlation is .074 for Factor 1 and .043 for Factor 4. An explanation based on age cannot explain the threshold nature of the relationship nor the failure to find an association for Factor 4 among navigators. Also, age is an essential component of the psychological dimension represented by aeronautical rating, suggesting that adjustment for age may also eliminate some of the effect that is of primary interest. This issue cannot be settled until factor scores can be related to stress measures that are less confounded with age.

We also investigated aircraft assignment as a possible stress-related variable. We divided pilots on the basis of their assignments, using a modification of the categorization scheme of Green and Swanborough (12). These categories included fighter/attack, bomber, transport, trainer, helicopter, and utility (including light reconnaissance/light transport). The small number of pilots in each category make appropriate comparisons difficult; only descriptive statistics will be presented. Data from navigators were omitted. The mean Factor 1 scores for each category are contained in Table 4, and Factor 4 scores are in Table 5. Figure 3 presents the means on Factor 1 by plane assignment, contrasting command pilots to all other pilots; and Figure 4, the means on Factor 4, contrasting command and senior pilots with pilots and students. The largest effect of aeronautical rating occurs in the fighter group, and the effect actually reverses in bomber pilots; but the small number of cases make these observations tentative. More detailed measures of mission stress may be necessary to construct categories that permit appropriate comparisons.

TABLE 4. SCORES ON FACTOR 1 BY AIRCRAFT ASSIGNMENT AND RATING

Group	N	Mean	Variance	SE
PILOTS				
Bomber pilots				
Command	10	-.18	.36	.19
Senior	12	.27	1.90	.40
Pilot	8	-.30	1.03	.31
Fighter Pilots				
Command	94	.39	1.56	.13
Senior	66	-.24	.82	.11
Pilot	29	-.13	.36	.11
Helicopter Pilots				
Command	11	.37	.32	.17
Senior	8	-.01	1.31	.40
Pilot	6	-.08	.21	.19
Transport Pilots				
Command	55	.32	.93	.13
Senior	35	-.41	.73	.14
Pilot	32	-.01	.74	.15
Trainer Pilots				
Command	54	.16	1.13	.14
Senior	38	-.11	1.43	.19
Pilot	42	-.40	.64	.12
Utility Pilots				
Command	11	.17	1.11	.32
Senior	7	-.75	.38	.23
Pilot	4	-.53	.64	.40

TABLE 5. SCORES ON FACTOR 4 BY AIRCRAFT ASSIGNMENT AND RATING

Group	N	Mean	Variance	SE
PILOTS				
Bomber pilots				
Command	10	.06	.52	.23
Senior	12	.14	.48	.20
Pilot	8	-.30	.65	.29
Fighter Pilots				
Command	94	.13	1.22	.11
Senior	66	.05	1.15	.13
Pilot	29	-.23	.68	.15
Helicopter Pilots				
Command	11	-.20	.97	.30
Senior	8	-.07	.36	.21
Pilot	6	.04	.47	.28
Transport Pilots				
Command	55	.17	.73	.12
Senior	35	-.23	.66	.14
Pilot	32	-.21	.92	.17
Trainer Pilots				
Command	54	.15	1.26	.15
Senior	38	.39	1.27	.18
Pilot	42	-.56	.91	.15
Utility Pilots				
Command	11	.02	1.00	.30
Senior	7	-.25	.68	.31
Pilot	4	-.12	.10	.16

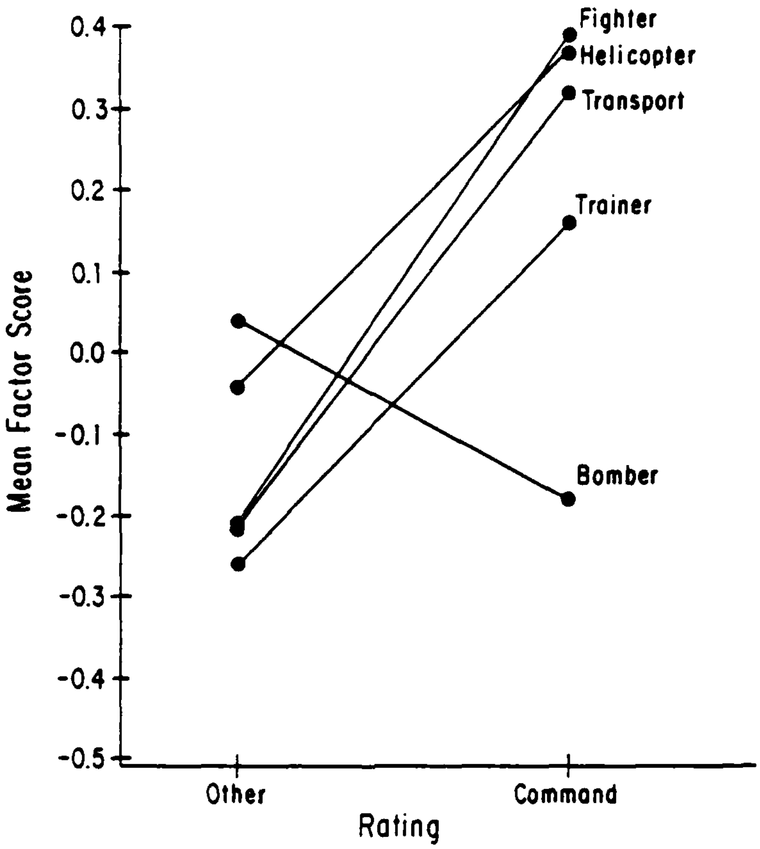

Figure 3. Factor 1 scores for pilots by rating and aircraft.

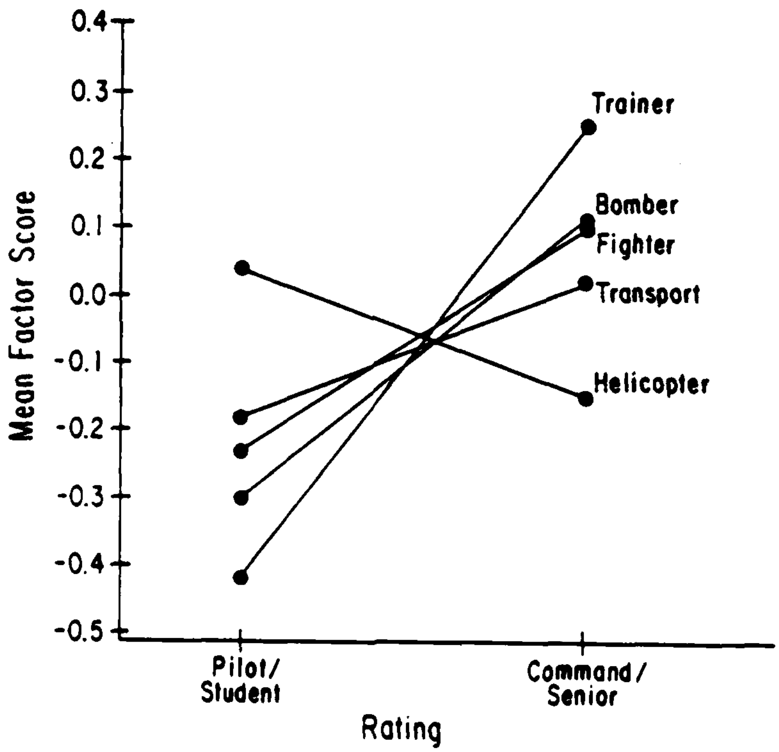

Figure 4. Factor 4 scores for pilots by rating and aircraft.

DISCUSSION

Several aspects of the findings from the analyses performed thus far suggest that Factors 1 and 4 have promise as biochemical profiles that reflect stress effects in operational aircrew. First and perhaps most compelling is the face validity of the clusters that emerged. One well-known concomitant of increased stress is increased sympathetic nervous system activation. Of the four measures that loaded on Factor 1, at least three (increased uric acid, triglycerides, and lipids ratio) would be expected to result from increased catecholamine release from the sympathetic nerves and adrenal medulla. With respect to Factor 4, lowered serum calcium, elevated fasting blood sugar, and elevated Na/K ratio are all known biological effects of cortisol. It was not until the 0900 cortisol value was added to the principal-components analysis, however, that these three variables clustered on Factor 4. Thus, in contrast to Factor 1, which reflects the participation of the sympathoadrenalmedullary system in the stress response, Factor 4 appears to reflect activation of the pituitary-adrenocortical axis.

Further strengthening our confidence in these factors as stress indicators is the congruence of the variables loading on these factors with the findings of previous military stress research. Inexperienced sailors on their first cruise on a fleet ballistic-missile submarine exhibited higher serum levels of both uric acid and cholesterol than the more experienced crewmembers (13)--both effects are reflected in Factor 1. Further suggesting the validity of the pattern of biochemical measures loading on Factor 1 is the finding (14) among a group of 10,000 middle-aged male civil service employees in Israel that serum uric acid levels are significantly positively correlated with serum cholesterol level and significantly negatively correlated with serum levels of HDL cholesterol--again a pattern that is strikingly mirrored in the pattern of loadings on Factor 1. The pattern of loadings on Factor 4, reflecting direct evidence of increased adrenocortical activation, is in strong agreement with the extensive research literature relating activation of the pituitary-adrenocortical axis to stress (1-5).

The increasing scores on both Factors 1 and 4 observed in the present data set as a function of increasing command level agree with the results of Miller et al. (3), which led them to pinpoint the "assigned role of leadership and responsibility" as a key factor in determining physiological responses to acutely stressful situations. Our findings serve both to provide support for this hypothesis and to support the validity of Factors 1 and 4 as stress indicators.

An interesting aspect of the changing distributions of factor scores with increasing aeronautical rating (Table 3) is the greater variance and positive skewness observed at the command level. This suggests that there is a greater preponderance of individuals with high factor scores as aircrews advance up the command chain to levels of greater responsibility. In future research it will be important to determine whether personnel with very high scores show poorer or better performance than those with low scores, as well as whether

they are prone to more health problems. We already have some evidence that both high cholesterol/HDL ratio and 0900 cortisol identify pilots with more severe coronary atherosclerosis (10). Are extremely high scores on the factors on which these parameters load (as identified in this study) useful in prospectively identifying aircrew at unusually high risk for developing coronary disease? If so, then follow-on studies could develop data leading to the incorporation of such measures into personnel selection procedures. Before this can be implemented, however, it will be important to determine whether high scores on these factors correlate with current performance, and even more important, whether they are predictive of subsequent performance and career paths.

Other aspects of the findings are tantalizing at this stage of the analyses, but the data are too sparse to warrant firm conclusions. Inspection of Table 4, for example, shows that among fighter pilots the variance of scores on Factor 1 increases significantly from pilot to command level-- an increase in variance not seen among aircrew assigned to other aircraft types. Does this increasing spread in distribution of Factor 1 scores among fighter pilots mean that some of them with very high scores are intolerant of stress? Or does it mean that they are more proficient in piloting these demanding aircraft? At the command level does the significantly lower Factor 1 score of bomber pilots in comparison to fighter pilots represent a real effect of the differing demands of flying the two types of aircraft? The small sample size in some of the aircraft groups precludes our having at this time too high a level of confidence in these apparent effects. Nevertheless, if confirmed in additional samples and if found to reflect real differences in performance levels and/or health risks, findings such as these could be very important in guiding personnel procedures aimed at selecting the most highly qualified and proficient pilots who will not fall prey to premature illness.

How do the present findings, from blood samples obtained "casually" in the course of routine clinical evaluations, relate to the various studies we have reviewed that show increased levels of biochemical stress indicators in settings of acute stress? We conclude that the high scores on Factors 1 and 4 in our data set suggest either that 1) even such casual blood sampling can indicate individuals who have been subjected to chronic stress over some indefinite period leading up to the time of sampling, or 2) certain individuals will display biochemical profiles indicative of stress simply because their psychological makeup makes them sensitive even to the moderate stresses encountered in everyday life. Some support for the latter view is provided by the observation that during the course of a typical working day, Type A men excrete more catecholamines in their urine than Type B men (15). On the other hand, the increased factor scores among pilots with increased levels of command responsibility suggest that chronically increased stress levels are also involved. Recent research (16) showing that both catecholamine and cortisol secretion increase as mental effort increases is consistent with our interpretation that increased command responsibility might lead to increased scores on Factors 1 and 4 via demands for chronically increased mental effort.

Near-term objectives designed to further validate these factors as stress indicators and to evaluate their potential utility as markers of attributes of individuals destined to become superior pilots include the following:

1. Seek additional samples with comparable biochemical data, to see if the factor structure identified in the current sample can be replicated.

2. Relate scores on Factors 1 and 4 to other available data on the current sample, to see if they correlate meaningfully with other face-valid stress indicators such as blood pressure and heart rate responses to exercise testing; psychological test data; and most importantly, subsequent career performance measures, health status, and incidence of accidents.

3. On new samples obtain biochemical data that would permit scores on Factors 1 and 4 to be correlated with concurrent measures of performance, subsequent performance and career paths, and risk of various diseases and accidents.

4. Evaluate scores on Factors 1 and 4 among pilots undergoing coronary angiography at USAFSAM, to determine whether factor scores correlate better with coronary atherosclerosis levels than do the individual variables loading on both factors, some of which are already known to correlate strongly with atherosclerosis levels.

5. Test the generality of these findings in other populations. The present analyses were based on data from a patient population, but future applications of the results will take place in nonclinical settings. To replicate this study on nonclinical personnel would be most desirable, ideally on pilots and navigators early in their training.

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